

(19) World Intellectual Property  
Organization  
International Bureau



10/522696



(43) International Publication Date  
12 February 2004 (12.02.2004)

PCT

(10) International Publication Number  
WO 2004/013096 A3

(51) International Patent Classification<sup>7</sup>: C07D 305/14, 493/00

(21) International Application Number:  
PCT/US2003/024666

(22) International Filing Date: 4 August 2003 (04.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/401,191 4 August 2002 (04.08.2002) US

(71) Applicant (for all designated States except US): NATURAL PHARMACEUTICALS INC. [US/US]; 100 Cummings Center, Suite 414-G, Beverly, MA 01915 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): JOHNSON, James, H. [US/US]; 6 Central Street, Merrimac, MA 01860 (US). GALLEGHER, Rex, T. [US/US]; 22 Old Town Road, Beverly, MA 01915 (US). WANG, Dasheng [US/US]; 17 Providence Rd., Westford, MA 01886 (US). JUCHUM, John, S. [US/US]; 315 The Heights at Cape Ann, Gloucester, MA 01930 (US).

(74) Agent: PARKER, Thomas, J.; Coudert Brothers LLP, 1114 Avenue of the Americas, New York, NY 10036 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
17 June 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND COMPOSITIONS FOR CONVERTING TAXANE AMIDES TO PACLITAXEL OR OTHER TAXANES

(57) Abstract: The invention relates to methods and compositions for converting taxane amides to paclitaxel or other taxanes. In one alternative embodiment, the present invention comprises; (i) selectively protecting at least one OH group of a taxane amide; (ii) contacting the taxane amide with a transition metal compound to reduce the amide; (iii) contacting the reduced amide with an agent capable of substantially removing the transition metal; (iv) contacting the reduced amide with a hydrolyzing amount of acid to form a taxane amine salt in solution; (v) adding a sufficient amount of solvent to solidify the amine salt; and (vi) converting the taxane amine salt into paclitaxel or other taxanes.

WO 2004/013096 A3

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/24666

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07D 305/14, 493/00  
US CL : 549/510

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 549/510

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAS-ONLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,319,112 A (KINGSTON et al) 07 June 1994.	1-12, 62-70, 101-109

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

14 November 2003 (14.11.2003)

Date of mailing of the international search report

21 APR 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

Taofiq A. Solola

Telephone No. (703) 308-1235

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/24666

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Confirmation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-12, 62-70, 101-109

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12, 62-70, 101-109, drawn to compounds.

Group II, claim(s) 13-33, drawn to a process of taxane salt from taxane imine.

Group III, claim(s) 34-61, 71-78, drawn to a process of making taxane mixture from taxane amide and transition metal.

Group IV, claim(s) 79, drawn to a process of making taxane imine from taxane amide.

Group V, claim(s) 80-100, drawn to a 2<sup>nd</sup> process of making taxane salt from taxane imine.

Group VI, claim(s) 110-112, drawn to a 2<sup>nd</sup> process of making taxane imine from taxane amide.

The inventions listed as Groups II-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the inventions are drawn to different processes of making the same or different products. Therefore, under PCT Rule 13.1 and 13.2, they lack the same or corresponding special technical features.

The inventions listed as Groups I and II-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the invention of group I is drawn to compounds while the inventions of groups II-VI are drawn to different processes of making compounds different from the compounds of group I. Therefore, under PCT Rule 13.1 and 13.2, they lack the same or corresponding special technical features.